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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/724,806	12/01/2003	Randy D. Blakely	VBLT:008USD1	3686

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EXAMINER	
BUNNER, BRIDGET E	
ART UNIT	**PAPER NUMBER**
1647	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/24/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/724,806	BLAKELY ET AL.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *29-32 and 35* is/are allowed.

6)☒ Claim(s) *33,34 and 36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 June 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment of 09 November 2006 has been entered in full. Claims 29-30 and 34-35 are amended.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 29-36 are under consideration in the instant application.

Withdrawn Objections and/or Rejections

1. The objection to claim 29 at pg 2-3 of the previous Office Action (09 August 2006) is *withdrawn* in view of the amended claim (09 November 2006).

2. The objections to the specification at pg 3 of the previous Office Action (09 August 2006) are *withdrawn in part* in view of the amended specification (09 November 2006). Please see section on Specification, below.

3. The rejection of claims 29-33 and 35 under 35 U.S.C. § 112, first paragraph (scope of enablement and written description) as set forth at pg 4-9 of the previous Office Action (09 August 2006) is *withdrawn* in view of the amended claims (09 November 2006).

4. The rejection of claims 29-35 under 35 U.S.C. § 112, first paragraph (written description) as set forth at pg 9-12 of the previous Office Action (09 August 2006) is *withdrawn* in view of the amended claims (09 November 2006).

5. The rejection of claims 29-34 under 35 U.S.C. § 112, second paragraph as set forth at pg 12-13 of the previous Office Action (09 August 2006) is *withdrawn* in view of the amended claims (09 November 2006).

6. The rejections of claims 29-34 under 35 U.S.C. § 102(b) and 102(a) as set forth at pg 13-14 of the previous Office Action (09 August 2006) are *withdrawn* in view of the amended claims (09 November 2006).

Sequence Compliance

7. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). **Specifically, the sequence disclosed in Figure 2 for ChCoT, *Limulus polyphemus,* is not accompanied by the required reference to the relevant sequence identifiers. Additionally, the specification discloses primer sequences at page 128 that are not accompanied by the required reference to the relevant sequence identifiers.** This application fails to comply with the requirements of 37 CFR 1.821 through 1.825. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825). It is noted that at pg 8 of the Response of 09 November 2006, Applicant indicated that an amendment to add the sequence for ChCoT, *Limulus polyphemus*, would be provided at a later date. The Examiner has yet to receive such an amendment.

Specification

8. The disclosure is objected to because of the following informalities:

8a. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: "POLYNUCLEOTIDE ENCODING A MURINE CHOLINE TRANSPORTER".

Appropriate correction is required.

The basis for this objection is set forth at pg 3 of the previous Office Action (09 August 2006). Although Applicant amended the title in the Response of 09 November 2006, it was amended to read "Polynucleotide encoding a mouse choline transporter cDNA". The Examiner wanted to clarify the title because a polynucleotide does not encode cDNA.

Claim Rejections - 35 USC § 112, second paragraph

9. Claim 33 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10. Claim 33 is rejected as being indefinite because it is not clear how a polynucleotide is comprised in a vector. (Please note that this issue could be overcome by amending the claim to recite, for example, "...wherein said polynucleotide is in a vector".)

Claim Rejections - 35 USC § 112, first paragraph

11. Claims 34 and 36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polynucleotide encoding a polypeptide comprising the amino acid sequence as set forth in SEQ ID NO: 4 and for an isolated polynucleotide comprising the nucleic acid sequence as set forth in SEQ ID NO: 3, does not reasonably provide enablement for a purified and isolated polynucleotide comprising a sequence identical or complementary to between 10 and 100 contiguous nucleotides of SEQ ID NO: 3 (claim 26). The specification is also not enabling for a recombinant vector or recombinant host cell comprising a DNA segment encoding any isolated murine choline transporter (claim 34).

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The basis for this rejection is set forth at pg 4-9 of the previous Office Action (09 August 2006).

Applicant's arguments (09 November 2006), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

(i) At pg 9 of the Response, Applicant traverses the rejection, but in the interest of advancing prosecution, states that claims 29, 30, 34, and 35 have been amended. Applicant also indicates that claim 36 is cancelled. However, claim 36 has not been cancelled and still reads upon fragments of SEQ ID NO: 3. As discussed in the previous Office Action, the specification does not teach any variants, fragments, or derivatives of the nucleic acid sequence of SEQ ID NO: 3. Further, the specification does not teach functional or structural characteristics of the polynucleotide variants, fragments, or derivatives in the context of a cell or organism. Certain positions in the polypeptide sequence are critical to the protein's structure/function relationship, e.g., such as various sites or regions directly involved in binding, activity, and in providing the correct three-dimensional spatial orientation of binding and active sites. However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the DNA and protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. A large quantity of experimentation would be required by the skilled artisan to generate the infinite number of derivatives recited in the claims and screen the same for activity. The specification's general

discussion of making and screening for variants constitutes an invitation to experiment by trial and error.

(ii) At pg 7-8 of the previous Office Action, the Examiner interpreted claims as reading on isolated host cells, as well as host cells in the context of a multicellular, transgenic organism and host cells intended for gene therapy, but incorrectly identified the claim numbers. Applicant did not specifically address this issue. So, for clarification, the Examiner has interpreted claim 34 as reading on an isolated host cell, as well as a host cell in the context of a multicellular, transgenic organism and a host cell intended for gene therapy. The specification of the instant application teaches that CHT gene product can be expressed in transgenic animals (for example pg 7, lines 28-29; pg 8, lines 1-8). However, there are no methods or working examples disclosed in the instant application whereby a multicellular animal with the incorporated mCHT gene of SEQ ID NO: 3 is demonstrated to express the mCHT polypeptide. The unpredictability of the art is *very high* with regards to making transgenic animals. For example, Wang et al. (Nuc. Acids Res. 27: 4609-4618, 1999; pg 4617) surveyed gene expression in transgenic animals and found in each experimental animal with a single "knock-in" gene, multiple changes in genes and protein products, often many of which were unrelated to the original gene. Likewise, Kaufman et al (Blood 94: 3178-3184, 1999) found transgene expression levels in their transfected animals varied from "full" (9 %) to "intermediate" to "none" due to factors such as "vector poisoning" and spontaneous structural rearrangements (pg 3180, col 1, 2nd full paragraph; pg 3182-3183). Therefore, it would have required undue experimentation for the skilled artisan to have made any and all transgenic non-human animals according to the instant invention.

The specification also discloses that nucleic acids encoding the mCHT polypeptide can be used for gene therapy (pg 3, line 22). However, the specification does not teach any methods or working examples that indicate a mCHT nucleic acid is introduced and expressed in a cell for therapeutic purposes. The disclosure in the specification is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. For example, the specification does not teach what type of vector would introduce the mCHT nucleic acid into the cell or in what quantity and duration. Relevant literature teaches that since 1990, about 3500 patients have been treated via gene therapy and although some evidence of gene transfer has been seen, it has generally been inadequate for a meaningful clinical response (Phillips, A., J Pharm Pharmacology 53: 1169-1174, 2001; abstract). Additionally, the major challenge to gene therapy is to deliver DNA to the target tissues and to transport it to the cell nucleus to enable the required protein to be expressed (Phillips, A.; pg 1170, ¶ 1). Phillips also states that the problem with gene therapy is two-fold: 1) a system must designed to deliver DNA to a specific target and to prevent degradation within the body, and 2) an expression system must be built into the DNA construct to allow the target cell to express the protein at therapeutic levels for the desired length of time (pg 1170, ¶ 1). Therefore, undue experimentation would be required of the skilled artisan to introduce and express a mCHT nucleic acid into the cell of an organism. Additionally, gene therapy is unpredictable and complex wherein one skilled in the art may not necessarily be able to introduce and express a mCHT nucleic acid in the cell of an organism or be able to produce a mCHT protein in that cell. (Please note that this issue could be overcome by amending the claim to recite, for example, "An isolated host cell...").

Proper analysis of the Wands factors was provided in the previous Office Action. Due to the large quantity of experimentation necessary to generate the infinite number of derivatives recited in the claims and possibly screen the same for activity, and to generate a transgenic animal expressing the mCHT protein and to introduce and express a mCHT nucleic acid in a cell of an organism for therapy; the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity and how to introduce a mCHT nucleic acid in the cell of an organism to be able produce that mCHT; the absence of working examples directed to same; the complex nature of the invention; the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function and the unpredictability of making transgenic animals and of transferring genes into an organism's cells; and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

12. Claim 36 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The basis for this rejection is set forth at pg 9-12 of the previous Office Action (09 August 2006).

Applicant's arguments (09 November 2006), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

Applicant traverses the rejection, but in the interest of advancing prosecution, states that claims 29, 30, 34, and 35 have been amended. Applicant also indicates that claim 36 is cancelled. However, claim 36 has not been cancelled and still reads upon fragments of SEQ ID NO: 3. As discussed in the previous Office Action, the claim does not require that the nucleic acid possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature. Thus, the claim is drawn to a genus of nucleic acid molecules. In this case, there is not even identification of any particular portion of the nucleic acid structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. Additionally, the description of one mCHT polynucleotide species (SEQ ID NO: 3) and one mCHT polypeptide species (SEQ ID NO: 4) is not adequate written description of an entire genus of functionally equivalent polynucleotides which incorporate all fragments of SEQ ID NO: 3. Even one skilled in the art could not envision the detailed chemical structure of all or a significant number of encompassed mCHT polynucleotides, and therefore, would not know how to make or use them. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of making. The claimed product itself is required. Therefore, only an isolated nucleic acid molecule consisting of the nucleic acid sequence of SEQ ID NO:3 and a nucleic acid molecule which encodes a polypeptide consisting of the amino acid sequence of SEQ ID NO:4, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph.

Claim Rejections - 35 USC § 102

13. Claim 36 is rejected under 35 U.S.C. 102(b) as being anticipated by Okuda et al. (Nat Neurosci 3(2): 120-125, 2000; Genbank Accession No. AB030947). The basis for this rejection is set forth for claims 29-34 and 36 at pg 13-14 of the previous Office Action (09 August 2006).

Okuda et al. teach an isolated "CHT1" polynucleotide that is 92.7% identical to the nucleic acid sequence of SEQ ID NO: 3 of the instant application. The CHT1 polynucleotide of Okuda et al. comprises a nucleic acid sequence that is identical to at least 134 contiguous nucleotides of SEQ ID NO: 3 of the instant application (see nucleic acids 1418-1551 of Okuda et al. and nucleic acids 1195-1328 of SEQ ID NO:3 of the instant application).

At pg 10 of the Response of 09 November 2006, Applicant indicates that claim 36 has been cancelled, therefore obviating the question of limited segments of homology. However, claim 36 has not been cancelled and still reads upon fragments of SEQ ID NO: 3. Thus, Okuda et al. anticipates claim 36.

14. Claim 36 is rejected under 35 U.S.C. 102(a) as being anticipated by Haga et al. (WO 0116315; 08 March 2001; see also pg 24-25 of CA 2382464 (Canadian translation of WO 0116315)). The basis for this rejection is set forth for claims 29-36 at pg 14-15 of the previous Office Action (09 August 2006).

Haga et al. teach an isolated murine polynucleotide that is 99.3% identical to the nucleic acid sequence of SEQ ID NO: 3 of the instant application (see SEQ ID NO: 7 of Haga et al.). The CHT1 polynucleotide of Haga et al. comprises a nucleic acid sequence that is identical to

over 100 contiguous nucleotides of SEQ ID NO: 3 of the instant application (see nucleic acids 356-1733 of Haga et al. and nucleic acids 356-1733 of SEQ ID NO:3 of the instant application).

At pg 10 of the Response of 09 November 2006, Applicant indicates that claim 36 has been cancelled, therefore obviating the question of limited segments of homology. However, claim 36 has not been cancelled and still reads upon fragments of SEQ ID NO: 3. Thus, Okuda et al. anticipates claim 36.

Conclusion

Claims 29-32 and 35 are allowable.

The post-filing date art made of record and not relied upon is considered pertinent to applicant's disclosure:

Ferguson et al. Proc Natl Acad Sci U S A 101(23):8762-8767, 2004 (lethal impairment of cholinergic neurotransmission in CHT knockout mice)

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (571) 272-0881. The examiner can normally be reached on 8:30-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BEB
Art Unit 1647
18 January 2007

Bridget E. Bunner

BRIDGET BUNNER
PATENT EXAMINER